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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,607	03/17/2004	Chaim M. Roifman	LYMF-P03-007	5885

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EXAMINER	
SACKEY, EBENEZER O	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 06/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/803,607	ROIFMAN ET AL.	
	Examiner	Art Unit	
	EBENEZER SACKEY	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12,14,21-31 and 36-39* is/are rejected.

7)☒ Claim(s) *13,15-20,32-35 and 40-43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-43 are pending.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 03/10/05 and 3/17/05 respectively is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of each of the 1449 is attached herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30, 31, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for leukemia, a lymphoma, a myeloma or carcinoma cancers, does not reasonably provide enablement for all cancers. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689.

To make clearer the lack of enablement for treatment of all cancer, extrinsic evidence is supplied by Draetta (Ann. Reports Med. Chem.), Draetta, G. and Pagano, M. in "Annual Reports in Medicinal Chemistry, Vol. 31", 1996, Academic Press, San Diego, p 241-246. Final sentence on page 246 "[a]lthough many still think about the need for a magic bullet as a cure for all cancers, our knowledge of the molecular mechanism underlying this disease make the prospect of developing such a universal cure very unlikely." Since no universal cure for cancer has been developed, it follows that there is no correlation between the assays relied upon by applicants and the ability to treat all cancers. Thus, those assays are not sufficient to enable the claim(s).

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Determining if any particular cancer would be treatable with Applicants' compounds would require clinical trials in each disease with each compound. Considering the hundreds of thousands of compounds covered by compounds and derivatives of formula (I) and the multitude of different cancers, this is a very large degree of experimentation. b) The direction concerning cancer treatment is found in pages 25-27. Applicants' *in vitro* assay described in page 27-28. Applicants describe no formulations, doses, or dosing schedules required to practice their invention. c) There are three working example of cancer treatment in man or animal in the specification. d) The claim rejected is drawn to clinical medicine and are therefore physiological in nature. e) The state of the art in cancer therapy is the remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the "cancer" category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases.

f) The artisan using Applicants invention would be a Board Certified physician in oncology with an MD degree and several years of experience. g) It is well established

that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The intractability of cancers generally is clear evidence that the skill level in this art is low relative to the difficulty of the task. h) The breadth of the claims include all of the hundreds of thousands of compounds of formula I as well as the presently unknown list of diseases embraced by each of the claims. Thus, the scope of the claims is broad.

Applicants' critical failure is the lack of a single specific cancer they intend to treat or inhibit and the complete lack of data showing efficacy of their compounds against that cancer. Cancers vary from those so benign that they are never treated to those so virulent that all present therapy is useless. The present specification says, in effect: here are the compounds and how to make them. You figure out what cancers they might be useful against. This is not the "immediate benefit to the public" required by *Cross et al. v. Iizuka et al* 224 USPQ 739, and *Nelson v. Bowler* 206 USPQ 881.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28, 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite a method of modulating cell proliferation. The meaning of "modulate", among others is to adjust or adapt to a certain proportion. However, from a reading of the specification, the intent of the claim is to treat cell proliferation not to adapt or adjust. Amending the claims to recite "treating" cell proliferation would obviate this rejection.

2. Claim 37 recites a compound capable of inhibiting cell proliferation. It is not entirely clear what that means.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-12 and 27, are rejected under 35 U.S.C. 102(b) as being anticipated by Wadsworth et al., (U.S.Patent number 30,47,606) or Phalanges et al., 4,950,467) or Taketani et al., (U.S.Patent number 5,196,147).

Applicants claim compounds of formula (I) and pharmaceutical composition and salt, solvates or hydrate thereof.

Wadsworth et al., disclose compounds and compositions which anticipate the instant claims when R^4 is $P(O)(OC_{1-6}alkyl)$, wherein R^1 is H, $R^2$and R^3 are each hydrogen. See reference compounds in column 1, line 68.

Phalanges et al., disclose compounds and compositions, which anticipate the instant claims when R^4 is $C(X)R^5$, wherein X is O: and R^5 is C_{1-6}alkoxy, and each of R^1, R^2 and R^3 are each hydrogen. See reference compounds in column 5, Preparation 13.

Taketani et al., disclose compounds and compositions, which anticipate the instant claims when R^4 is $C(X)R^5$, wherein X is O: and R^5 is OH, and each of R^1, R^2 and R^3 are each hydrogen. See reference compounds in column 15, Example 7.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 21 and 22 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 22 of prior U.S. Patent No. 6,800,659. This is a double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made..

I. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

II. Claims 1-3, 6-12, 14 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wadsworth et al. (U.S.Patent number 3,047,606) or Taketani et al. (U.S.Patent number 5,196,147) or Phalangas et al. (U.S.Patent No. 4,950,467).

Applicants claim compounds, composition and methods of using formula (I) in treating disease state. The substituents are as defined in the claims.

Determination of the scope and content of the prior art (M.P.E.P.. §2141.01)

Wadsworth et al. disclose compounds, which are similar to the instantly claimed compounds. See the entire publication, for example column 1, lines 55-72.

Taketani et al. disclose compounds, which are similar to the instantly claimed compounds. See the entire reference especially column 8, lines 10-59, all the various species disclosed therein, column 15, Example 7 etc.

Phalagas et al. disclose compounds similar to the instantly claimed compounds. See the entire reference, especially Preparations 13, 14, 15 and 16.

Ascertainment of the difference between the prior art and the claims (M.P.E.P.. §2141.02)

The difference between the instant compounds and composition and that the references herein lie in the generic description of the compounds and composition.

Finding of prima facie obviousness---rational and motivation (M.P.E.P.. §2142-2143)

The claimed compounds and composition would have been obvious because one of ordinary skill in the art would have been motivated to either prepare compounds and compositions embraced by the reference's genus or prepare positional isomers or homologs of the compounds taught in the references to arrive at the instantly claimed compounds and composition with the expectation that the resulting compounds and composition would have similar activity to that taught by the references. In order to

establish patentability in positional isomers, there must at least be a comparative showing establishing distinguishing characteristics allegedly showing that the claimed compounds are unobvious. Ex Parte Henkel, 130 USPQ 474 (1960). The instantly claimed compounds and compositions would therefore have been suggested to one of ordinary skill. Additionally, the motivation to make the claimed compounds and composition derives from the expectation that structurally similar compounds are generally expected to have similar properties and similar utilities. *In re Gyurik*, 596, F2d. 1012, 201 USPQ 552 (CCPA), 1979.

Claims 13, 15-20, 32-35 and 40-43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

It is noted that there are (2) claims 41. This appears to be a typographical error. Correction is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to E. Sackey whose telephone number is (571) 272-0704. The examiner can normally be reached on Monday-Friday from 7:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

EOS
May 27, 2005

T. Solola
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Art Unit 1626, Group 1600
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